

Peanut challenge: a retrospective study of 140 patients

F. PUCAR*, R. KAGAN†, H. LIM‡ and A.E. CLARKE*†

*Divisions of *Allergy/Clinical Immunology and ‡Clinical Epidemiology, Montreal General Hospital and †Division of Allergy/Clinical Immunology, Montreal Children's Hospital, McGill University, Montreal, Quebec, Canada*

Summary

Background Accurate diagnosis of peanut allergy is essential given that it is a lifelong and potentially fatal food allergy. Diagnosis relies on patient history, prick skin test (PST), and in many situations, food challenge. More information is required on the safety of food challenge and the informational value of a PST.

Objectives Primary: to assess the safety of peanut challenges. Secondary: to estimate the sensitivity, specificity, and the positive and negative predictive values of PST to peanut performed in those who underwent a peanut challenge.

Methods A retrospective study of peanut challenges performed at a tertiary care paediatric hospital allergy clinic between January 1994 and November 1998.

Results Of the 140 peanut challenges performed on 140 patients, 18 were positive. The most frequent adverse clinical effects of positive peanut challenges were: urticaria, oropharyngeal irritation, rhinitis, vomiting and abdominal pain. Among the 18 patients who had a positive result, 10 required medical treatment (antihistamines, $\pm$ epinephrine, $\pm$ salbutamol) to control the allergic reaction. The sensitivity, specificity, and the positive and negative predictive values of PST to peanut in this group of children undergoing a peanut challenge were 100%, 62.3%, 28.1% and 100%, respectively.

Conclusions Given the poor positive predictive value and specificity of PST, a peanut challenge is usually required to diagnose peanut allergy with certainty when the PST is positive. In cases of a clear history of anaphylaxis to peanut and a positive PST, challenges are unwarranted. When the history is strongly suggestive and the PST is borderline positive, i.e. 3 or 4 mm, peanut challenge is generally necessary to confirm the diagnosis. Given the excellent negative predictive value and sensitivity of PST, a blinded peanut challenge is usually unnecessary in the context of a negative PST except for patients with a history strongly suggestive of immediate hypersensitivity. These patients should be individually assessed for the need to undergo a blinded challenge. The peanut challenge is a useful and safe diagnostic tool when performed by qualified personnel under appropriate conditions.

Keywords: peanut allergy, children, food challenge, sensitivity, specificity, predictive value, prick skin test

Clinical and Experimental Allergy, Vol. 31, pp. 40–46. Submitted 26 October 1999; revised 14 January 2000; accepted 23 May 2000.

Introduction

Peanut allergy is a serious food allergy and potentially fatal [1–3]. Although disputed, an increased prevalence in the

population has been reported [4–6] and is currently estimated at between 0.4% and 0.7% [7–9]. Given the heightened public awareness of the potential danger of food allergies, it is not surprising that the demand for food allergy assessment has increased [4]. Considering the strict dietary precautions that must be followed by peanut allergic individuals and the attendant psychological consequences

Correspondence: Ann Clarke, Division of Clinical Epidemiology, Montreal General Hospital, 1650 Cedar Avenue, Montreal, Quebec, Canada H3G 1A4. E-mail: anncl@bic.mni.mcgill.ca

Table 1. Peanut challenge prototypes

Open food challenge	Step 1: 250–500 mg of peanut butter Step 2: 8–10 g of peanut butter on crackers – > Observe for 2 h
Single-blind food challenge	Step 1: Rub peanut on lips (optional) Step 2: Placebo Step 3: 10–50 mg of peanut flakes hidden in jelly or apple sauce Step 4: 250 mg of peanut flakes Step 5: 500 mg of peanut flakes Step 6: 1 g of peanut flakes Step 7: 8–10 g of peanut flakes – > Observe for 2 h

[10], diagnostic accuracy is essential. However, there are limited data on the sensitivity, specificity and predictive value of prick skin testing (PST) to peanut [11–14]. Prick skin testing to peanuts has been reported to have a sensitivity of >90% [11,13], specificity of about 60% [11,13], positive predictive accuracy of about 50% [11–13], and negative predictive accuracy of >95% [11–13]. In the presence of a convincing medical history and a positive PST, diagnosis of peanut allergy is straightforward. Likewise, a history inconsistent with an IgE-mediated hypersensitivity reaction and a negative PST almost completely excludes a peanut allergy. However, for patients in whom a diagnosis cannot be established with certainty by history and PST, a peanut challenge is then the gold standard for proper diagnosis. In this retrospective study, we present the results of peanut challenges performed among a paediatric population, assessing both the safety of the procedure as well as the sensitivity, specificity and predictive values of the PST in this group of patients.

Subjects and methods

Through a chart review of children attending the Montreal Children's Hospital allergy clinic between January 1994 and November 1998, 140 patients who underwent oral peanut challenges to assess a possible IgE-mediated hypersensitivity to peanut were identified. Except in very rare cases, children with a convincing history of an allergic reaction and a positive PST to peanut ≥ 5 mm were not challenged.

At the physician's discretion, the challenges were either open (peanut not hidden) or single-blind (only the child was blinded to the composition of the ingested food). Open challenges were, with a single exception, performed only if the PST was negative. In a single case, an open challenge was performed when the PST was 3 mm and the patient had a history questionable of an allergic reaction. Blind

challenges were performed in all other cases where the PST was positive.

Food challenges were performed according to previously published protocols [15–17]; however, the number of steps and dosing of each challenge were left to the discretion of the treating allergist. The basic design of the challenges was similar for all children (Table 1) and all concluded by open ingestion of peanut butter or equivalent peanut containing foods. In the blind challenge, peanut flakes served as the source of peanut; almond or coconut flakes served as the placebo and both were disguised in either apple sauce or grape jelly. Almond flakes were used in children who were known not to be nut allergic and are the preferred placebo because of their similarity in texture to peanut flakes. Placebos were given as the second step in the multidose challenge procedure and were variably interspersed with peanut throughout the challenge at the discretion of the supervising nurse, usually in circumstances where the peanut elicited subjective symptoms.

Prior to the challenge, patients were instructed to avoid antihistamines for at least 96 h and β -agonists for at least 12 h. The initial dose of peanut (or placebo) was 10–50 mg and, if tolerated, the dose was increased in the following fashion (e.g. 100 mg, 250 mg, 500 mg, 1 g, 5 g) every 20 min until a dose of 5–10 g was reached. The starting dose varied with the clinical history, where the initial amount of peanut chosen was unlikely to elicit a reaction even in exquisitely sensitive patients [17]. Twenty minutes was usually a sufficient interval for allergic symptoms to occur; in rare cases where the patient reported that the previous reaction(s) to peanut developed >20 min after ingestion, the dosing interval was increased.

Prior to the challenge, children were examined by the treating physician and the challenge was deferred if there was current or recent wheezing, i.e. within the previous 24 h. At baseline and between each dose, blood pressure and heart and respiratory rate were recorded and the patient

was queried on and observed for any signs/symptoms suggestive of an IgE-mediated allergic reaction. Following a negative challenge, the observation time period was usually 2 h. In the presence of a positive challenge, this observation period varied, but was at least 2 h following complete stabilization of the patient and usually 4 h following the last dose of peanut.

The PST to peanut was performed according to a standard technique and the results were expressed in millimetres of wheal and flare. The allergenic extract used (almost exclusively, except for a short period when it was unavailable) was a commercially prepared product produced and distributed by the Bayer Company. Histamine (1 mg/mL) and physiological saline served as positive and negative controls, respectively. A PST was considered positive if it produced a wheal diameter of at least 3 mm greater than the negative control within 15 min of placement. A PST of 3 or 4 mm greater than the negative control was interpreted as borderline positive. In the cases where the history was suggestive and the PST was negative with the commercial extract, the PST was usually repeated with either the peanut soaked in saline or peanut butter.

The 140 children who underwent peanut challenge were divided into four groups based on chart review: 'suggestive history', 'questionable history', 'negative history' and 'never exposed'. The 'suggestive history' group included patients with signs/symptoms occurring within 90 min after peanut exposure, either by ingestion or contact, that were probably IgE-mediated but who had a negative or borderline positive PST to peanut. As noted previously, those patients with a 'suggestive history' and a positive PST ≥ 5 mm were assumed to be at substantial risk of anaphylaxis if re-exposed to peanut and hence were not challenged. These patients are therefore not included in this review. There are two patients with a 'suggestive history' and a PST ≥ 5 mm who were challenged. In one case, the parents refused to accept that the child was peanut allergic and in the second, the child had previously had a negative PST performed with a less reliable extract, but when repeated on the day of the challenge with a more reliable extract (Bayer), it was positive with 5 mm of induration.

Signs and symptoms considered to be consistent with an IgE-mediated reaction included pruritus, urticaria, flushing, rhinoconjunctivitis, angioedema, throat tightness, gastrointestinal complaints, breathing difficulties (other than wheeze), wheeze, cyanosis, or circulatory collapse [3]. To be certain that it was peanut and not another food product responsible for the symptoms, the history had to be that of isolated ingestion of peanut or of a meal containing peanut and foods routinely tolerated. Furthermore, although allergic reactions have been reported up to several hours after ingestion, this is infrequent (3%) [3] and these

reactions were also not considered as consistent with a suggestive history.

The 'questionable history' group consisted of patients with a history which was somewhat atypical for an IgE-mediated reaction because of, for example, the type of symptoms, the time of their appearance, their persistence for several days and/or their inconsistent provocation by peanut exposure.

The 'negative history' group included patients reporting no prior adverse reaction to peanuts but who recently presented with a possibility and/or concern of a peanut allergy (e.g. recently discovered they had a nut allergy, had a positive PST to peanuts, or had experienced idiopathic anaphylaxis).

Finally, the 'never exposed' group consisted of patients with a personal or family history of food allergy(ies), but who had not knowingly ingested peanut or peanut containing products. For each group, the results of the peanut challenges were then expressed in the context of the PST results.

Allergic signs and symptoms induced by the challenge and medications administered will be described in the Results section. The sensitivity, specificity and predictive values of the PST with 95% confidence intervals were calculated.

Results

Of the 140 patients who underwent an oral peanut challenge, 28 challenges were open and 112 were single-blind. The challenges were performed on 60 girls and 80 boys, ranging in age from 15 months to 17 $\frac{1}{2}$ years at the time of the challenge, median age 5.2 years, mean age (standard deviation) 6.2 (3.7) years. None of these patients had experienced circulatory collapse with previous peanut exposure. Six children had experienced laryngeal discomfort on previous peanut exposure, 14 had experienced respiratory symptoms including dyspnea, cough, and/or wheezing, and 1 had anaphylaxis. Eighteen of the 140 challenges (12.9%; 7 girls and 11 boys) were positive.

Figure 1 shows the subject distribution based on history and PST results. Forty-seven had a 'suggestive history', 57 had a 'questionable history', 14 had a 'negative history', and 22 patients were 'never exposed'. Seventy-six children had a negative PST for peanut and 64 had a positive PST. Among the subjects with a negative PST, none had a positive peanut challenge. Among those with a positive PST, 18 had a positive peanut challenge. All of these 18 patients with a positive peanut challenge had a PST wheal of ≥ 5 mm (Fig. 2). There were, however, nine of 17 patients with a large positive skin test, i.e. ≥ 10 mm, who had a negative peanut challenge.

It should be noted that only four patients with a 'suggestive history' and positive PST underwent a peanut

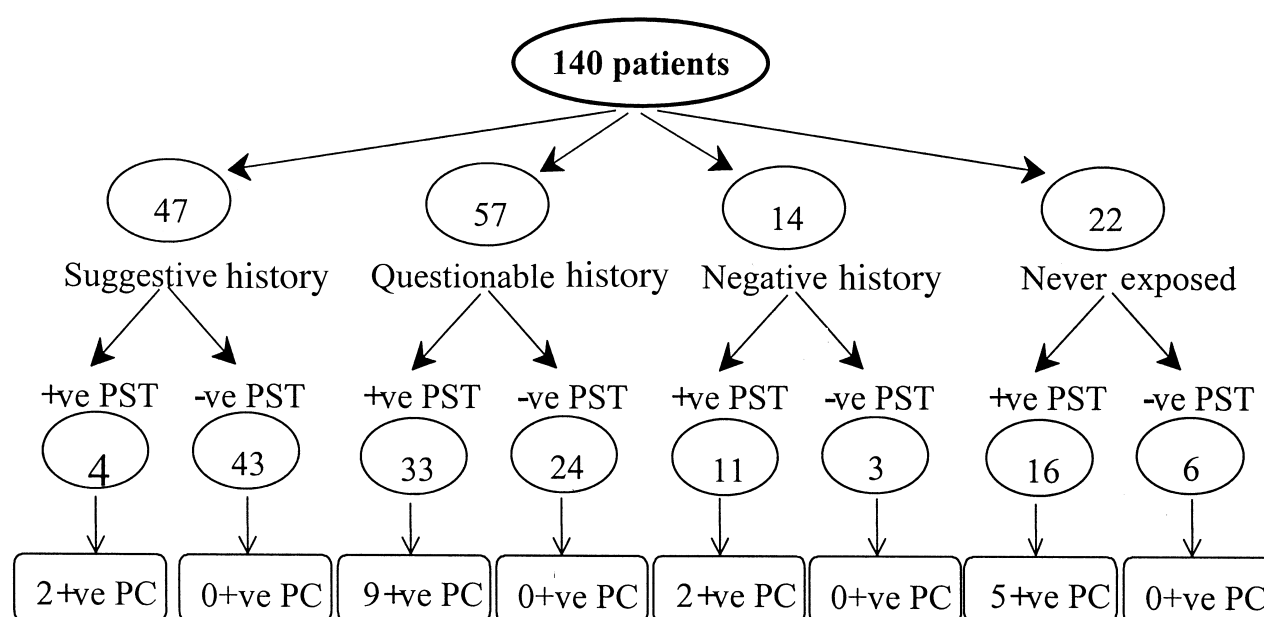


Fig. 1. Stratification of patients undergoing peanut challenge (PC) by history and prick skin test (PST) results.

challenge. Of these four, two had a PST wheal less than 5 mm and these two had a negative challenge. One patient with a 'suggestive history' and PST result of 9 mm who underwent a challenge did so because the child's parents were not convinced of the diagnosis of peanut allergy and were reluctant to avoid peanut products; the other originally had a negative PST which, upon repeating with Bayer extract the day of the challenge, was positive. These two children had positive challenges. Almost all children seen at our centre with a 'suggestive history' and positive PST ≥ 5 mm were not challenged as the risk of anaphylaxis with re-exposure was considered to be substantial.

During the peanut challenge, no life-threatening reactions occurred. Table 2 shows the clinical manifestations that led to discontinuation of the procedure. Allergic signs, listed in descending order of frequency, included urticaria, oropharyngeal irritation, rhinitis, vomiting and abdominal pain. Treatment was required to control the allergic reaction in 10 patients: antihistamines only for six patients, antihistamines and epinephrine for three patients, and antihistamines, epinephrine and salbutamol for one patient. No child required transfer to a specialized unit. All were successfully treated and were discharged home within a few hours following the allergic reaction.

Given that in children, the adverse effects of epinephrine are so minimal, any reaction which is judged to be even potentially moderate receives epinephrine. Bearing this practice in mind, it was still only administered four times in 140 challenges. In one case, a patient presented with neck and face urticaria without other associated symptoms

90 min after leaving the hospital following a negative challenge and 3–4 h after the last dose of peanut. The urticaria was not observed by the medical staff, but the mother administered a few doses of antihistamine to the child. Consequently, this challenge was considered positive. It would, however, have been useful to have repeated this challenge with a longer period of observation or administration of the placebo and peanut on separate days.

In our patient population of children undergoing peanut challenge, the sensitivity and specificity (95% confidence interval) of the PST (Table 3) was 100% (0.846–1.00) and

Table 2. Clinical manifestations reported during 18 positive peanut challenges

Manifestation	Number of patients
Urticarial rash	10
Oropharyngeal discomfort (without obvious angioedema)	9
Rhinitis	7
Vomiting	7
Abdominal pain or cramps	6
Facial flushing	4
Cutaneous pruritus	3
Cough	3
Wheezing without dyspnea	2
Ocular pruritus	2
Slight angioedema of the inferior lip	1

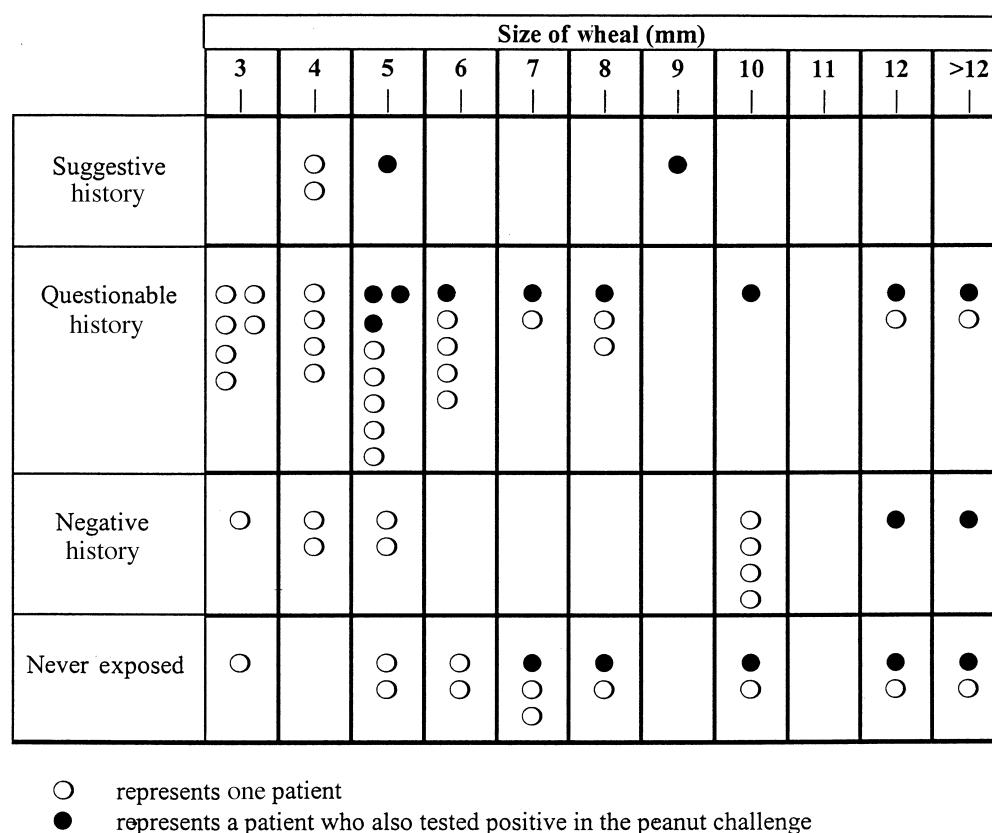


Fig. 2. Distribution of 64 patients with positive PST.

62.3% (0.531–0.709), respectively. The positive predictive value was 28.1% (0.176–0.407) and negative predictive value was 100% (0.961–1.00).

Discussion

The blind oral food challenge is the gold standard for diagnosis of food allergy. This test is not benign, as systemic allergic reactions can be induced. It is imperative

Table 3. Characteristics of Prick Skin Tests (PST) for Peanut Allergy

		Peanut oral challenge		Total
		+	–	
PST	+	18	46	64
	–	0	76	76
Total		18	122	140

Sensitivity: $18/18 = 100\%$

Specificity: $76/122 = 62.3\%$

Positive predictive value: $18/64 = 28.1\%$

Negative predictive value: $76/76 = 100\%$

therefore that the safety of these challenges be reported. This is especially relevant for peanuts, where even small amounts, in highly sensitized individuals, can precipitate allergic manifestations. Additionally, before deciding if such a challenge is indicated, the informational value of the peanut PST must be known.

Individuals are frequently considered peanut allergic solely on the basis of a positive peanut PST. Given the dietary and psychological implications of a diagnosis of peanut allergy, the clinical significance of a positive PST must be fully understood. Diagnosis of peanut allergy on the basis of a positive peanut PST alone may result in incorrect labelling of patients and unnecessary adherence to severely restricted diets. In our cohort of patients, the positive predictive value of the peanut PST was only 28.1%, indicating that only 28.1% of patients with a positive PST were actually peanut allergic as determined by the peanut challenge.

This low positive predictive value emphasizes the importance of performing a peanut challenge in all patients with a positive PST except in circumstances where the history is compatible with an IgE-mediated hypersensitivity. Among those with a 'suggestive history', and positive PST ≥ 5 mm, the risk of anaphylaxis with peanut re-exposure

was considered too great to perform a challenge. However, we have shown that of the two patients with a 'suggestive history' and positive PST < 5 mm, neither had a positive challenge. This suggests that patients with a 'suggestive history' and borderline positive PST would benefit from a peanut challenge prior to labelling the child as truly peanut allergic. Given the high number of false positive results with the peanut PST, the specificity is therefore low; in our sample it was 62.3%.

In our study, all patients with a negative PST had a negative challenge irrespective of the clinical history, yielding a negative predictive value of the peanut PST of 100%. Practically, this suggests that a negative PST, properly performed with a reliable, commercially available peanut extract, almost completely excludes a peanut allergy. Nevertheless, in certain situations, such as reassuring the patient and/or parent and/or physician, an open peanut challenge may be performed in a safe environment. Given the low number of false negatives with the peanut PST, the sensitivity of the PST is therefore high (100% in our sample), indicating its high probability of detecting all subjects who are potentially peanut allergic.

We recognize that these test characteristics cannot be applied directly to the general population of patients being evaluated for peanut allergy. The 140 subjects represent a subgroup among all the patients skin-tested for possible peanut allergy at the Montreal Children's Hospital allergy clinic over a 5-year period. Generally, because of the substantial risk of anaphylaxis, patients with a suggestive history of peanut allergy and a positive PST are not offered oral challenges and are considered peanut allergic. By including these patients, the positive predictive value of the PST would increase. Similarly, the specificity would probably increase if all patients with an atypical history of IgE-mediated peanut hypersensitivity and a negative PST underwent a peanut challenge. Despite our selected population, our data describing the characteristics of peanut PST are similar to results already present in the literature [11].

Although we have shown that all children with a PST < 5 mm had a negative challenge, there were nine of 17 children with a PST ≥ 10 mm who also had a negative challenge. None of these children, however, with a PST ≥ 10 mm had a suggestive history of peanut allergy. In those children with a suggestive history (albeit in our study, few were challenged), all with a positive PST ≥ 5 mm had a positive challenge. Establishing a threshold value for a peanut PST above which a peanut challenge is not necessary is an important question which cannot be answered definitively by our work which is a report of our clinical experience. Further studies are needed before a positive PST, in the context of the history of prior peanut exposure, can reliably predict the outcome for future

peanut exposure and obviate the need for peanut challenge. Hill *et al.* [18] have observed in 95 peanut challenges that a mean wheal size of ≥ 8 mm indicates a high probability of a positive challenge. However, the history of prior peanut exposure is not detailed. Hourihane *et al.* [19] compared 15 children with resolved peanut allergy with 15 with persistent peanut allergy. Of the 'resolvers', all had PST < 6 mm whereas all 'persisters' had PST ≥ 6 mm.

Although the double-blind, placebo-controlled challenge is advocated as the gold standard for the diagnosis of food allergy [15], it is time consuming and labour intensive, requiring one person to prepare the placebo/active agent and another to administer them. The placebo and active challenge can then be conducted sequentially and on separate days or approximately equal doses of placebo and the active agent can be randomly intermingled over the course of a day [17,20,21]. In most cases, we have conducted a single-blind placebo-controlled peanut challenge, interspersing placebo with peanut. Considering the young age of our patient population, our limited resources, and the long waiting list at our institution to undergo a food challenge, it was impractical and unfeasible to perform sequential challenges or a day-long challenge on each patient. The single-blind placebo-controlled challenge is considered a useful, practical alternative [20,21].

The open challenge was performed only in those children with a negative PST (with a single exception where a child had a PST of 3 mm). In most cases, it involved only two or three steps with rapid increase in the amount of peanut consumed. These challenges were performed because although the treating physician felt quite confident that the child was not peanut-allergic, the parents and children needed reassurance that peanut and peanut-containing foods could safely be re-introduced. Only one of the 28 open challenges was positive, with the child having a few perioral hives which did not require treatment. Although the PST in this positive challenge had been negative prior to the challenge, when repeated after the challenge with the Bayer extract (as noted previously), it became positive at 5 mm.

Our definition of peanut allergy was based on a recent study showing that 93% of subjects reported reactions within 30 min and only 3% reported adverse reactions more than 1 h after peanut ingestion [3]. Although we have accepted an interval of up to 90 min after peanut ingestion in defining a suggestive IgE-mediated reaction, only one patient in this group reported a reaction after 1 h (swollen lips and generalized urticaria).

Reviewing the positive peanut challenges, it is interesting to note that five patients were never knowingly exposed to peanut (or food containing peanut) and had their first clinical reaction during the peanut challenge. Five other patients had their first adverse reaction during their first known exposure to peanut and this hypersensitivity was

subsequently confirmed during the food challenge (data not shown). Developing peanut hypersensitivity with the first exposure is well described in the literature [3]. It should be recognized that in some cases parents or patients had probably forgotten a previous peanut exposure or parents were unaware of a previous peanut exposure given by other caregivers such as grandparents, babysitters or friends. However, the possibility of sensitization through breast milk or perhaps *in utero* has been suggested [5]. Our data support the idea that sensitization and clinical reactions to the first known exposure to peanut occur.

In our study, 22 patients who had not knowingly ingested products containing peanut were offered an oral challenge because of a personal or family history of food allergy. Six patients had a negative PST whereas 16 had a positive PST. Among these 16 patients with a positive PST, five had a positive oral challenge. Thus, despite the absence of any known sensitization, 31.3% [5/16] of the children with a positive PST but who had never eaten peanuts, had a clearly demonstrable peanut allergy. Given that personal and family history appear to be significant risk factors for developing peanut allergy, it seems appropriate to offer peanut PST to children with an atopic background.

In conclusion, a peanut challenge performed by qualified personnel, in a controlled environment, is safe and valuable. The peanut PST remains an efficient diagnostic tool for the detection and the exclusion of such an allergy. Accurate diagnosis is essential to avoid the burden of peanut allergy and in many situations the food challenge will provide the only definitive answer.

Acknowledgements

The authors wish to thank the nurses (Andrée Turenne, Janet Morrison and Claire Guay) and physicians (Christine Leytenji, Bruce Mazer, Elaine Medoff and Francisco Noya) affiliated with the Division of Allergy/Clinical Immunology at the Montreal Children's Hospital, Lawrence Joseph PhD for helpful discussions, and Jennifer Gardner for her expert secretarial assistance. This study was supported by grants from the Research Institutes of the Montreal General and Montreal Children's Hospitals. Dr Clarke is a Junior Clinician Scholar of the Fonds de la Recherche en Santé du Québec.

References

- 1 Sampson HA, Mendelson L, Rosen JP. Fatal and near-fatal anaphylactic reactions to food in children and adolescents. *N Engl J Med* 1992; 327:380–4.
- 2 Yunginger JW, Sweeney KG, Sturner WQ et al. Fatal food-induced anaphylaxis. *JAMA* 1988; 260:1450–2.
- 3 Hourihane J O'B, Kilburn SA, Dean P et al. Clinical characteristics of peanut allergy. *Clin Exp Allergy* 1997; 27:634–9.
- 4 Ewan PW. Clinical study of peanut and nut allergy in 62 consecutive patients: new features and associations. *BMJ* 1996; 312:1074–8.
- 5 Hourihane J O'B, Dean TP, Warner JO. Peanut allergy in relation to heredity, maternal diet, and other atopic diseases: results of a questionnaire survey, skin prick testing, and food challenges. *BMJ* 1996; 313:518–21.
- 6 Sampson HA. Epidemiology of food allergy (review). *Pediatr Allergy Immunol* 1996; 7:42–50.
- 7 Tariq SM, Stevens M, Matthews S et al. Cohort study of peanut and tree nut sensitisation by age of 4 years. *BMJ* 1996; 313:514–7.
- 8 Sicherer SH, Munoz-Furlong A, Burks AW et al. Prevalence of peanut and tree nut allergy in the US determined by a random digit dial telephone survey. *J Allergy Clin Immunol* 1999; 103:559–62.
- 9 Emmett SE, Angus FJ, Fry JS et al. Perceived prevalence of peanut allergy in Great Britain and its association with other atopic conditions and with peanut allergy in other household members. *Allergy* 1999; 54:380–5.
- 10 Primeau M-N, Kagan R, Joseph L, Lim N, Dufresne C, Duffy C, Prekal D, Clarke AE. The psychological burden of peanut allergy as perceived by adults with peanut allergy and the parents of peanut allergic children. *Clin Exp Allergy* 2000; 30:1135–43.
- 11 Sampson HA, Albergo R. Comparison of results of skin tests, RAST and double-blind, placebo-controlled food challenges in children with atopic dermatitis. *J Allergy Clin Immunol* 1984; 74:26–33.
- 12 Bock SA, Atkins FM. Patterns of food hypersensitivity during sixteen years of double-blind, placebo-controlled food challenges. *Pediatr* 1990; 117:561–7.
- 13 Sampson HA. Comparative study of commercial food antigen extracts for the diagnosis of food hypersensitivity. *J Allergy Clin Immunol* 1988; 82:718–26.
- 14 Burks AW, James JM, Hiegel A et al. Atopic dermatitis and food hypersensitivity reactions. *J Pediatr* 1998; 132:132–6.
- 15 Bock SA, Sampson HA, Atkins FM et al. Double-blind, placebo-controlled food challenge (DBPCFC) as an office procedure: a manual. *J Allergy Clin Immunol* 1988; 82:986–97.
- 16 Niggemann B, Wahn U, Sampson HA. Proposals for standardization of oral food challenge tests in infants and children. *Pediatr Allergy Immunol* 1994; 5:11–3.
- 17 Hourihane J O'B, Kilburn SA, Nordlee JA et al. An evaluation of the sensitivity of subjects with peanut allergy to very low doses of peanut protein: a randomized, double-blind, placebo-controlled food challenge study. *J Allergy Clin Immunol* 1997; 100:596–600.
- 18 Hill DJ, Sporik R, Hosking CS. The value of allergen skin testing in predicting adverse reactions to foods in children: a specific marker. *J Allergy Clin Immunol* 1999; 103:S99.
- 19 Hourihane J O'B, Roberts SA, Warner JO. Resolution of peanut allergy: case-control study. *BMJ* 1998; 316:1271–5.
- 20 Daniels MA. Oral diagnostic challenges. *Immunol Allergy Clin North Am* 1999; 19:75–82.
- 21 Metcalfe DD, Sampson H, Simon R. Food Allergy. Adverse Reactions to Foods and Food Additives 2nd edn. Oxford: Blackwell Science, 1997.